



PATENT  
Attorney Docket No.: 11641/167  
U.S. Appn.. No. 10/688,905

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Gregory L. KIRK et al.  
Title: BIOLOGICAL ASSAYS USING GRADIENTS FORMED IN  
MICROFLUIDIC SYSTEMS  
Application No.: 10/688,905  
Filing Date: October 21, 2003  
Docket No.: 11641/167  
Group Art Unit: 1744  
Examiner: Bowers

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**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

SIR:

In response to the Advisory Action of August 8, 2007, Applicants request review of the Final Rejection of June 4, 2007 in the above-identified application. A notice of appeal is being filed concurrently with this request. This review is requested for the reasons stated below.

### **Summary of Rejections**

Claims 1, 9 and 10 stand rejected under 35 U.S.C. 103(a) as being allegedly obvious over U.S. Patent 5,744,366 to Kricka ("Kricka") in view of U.S. Patent 6,251,343 to Dubrow ("Dubrow"). Claims 1, 2, 9-11, 17, 18, 22 and 24 stand rejected under 35 U.S.C. 103(a) as being allegedly obvious over U.S. Patent 6,238,874 to Jarnigan ("Jarnigan") in view of Dubrow. Claims 3-5 stand rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by Kricka or Jarnigan in view of Dubrow and U.S. Patent 5,284,753 to Goodwin, Jr. ("Goodwin"). Claims 3-5, 12, 13 and 19-23 stand rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by Jarnigan and Dubrow in view of Kennedy "Motility and chemotaxis..." and/or Shonnard "Hydrodynamic effects...". Claims 3 and 6-8 stand rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by Kricka or Jarnigan, and in further view of Dubrow and U.S. Patent 6,705,357 to Jeon ("Jeon"). Claims 14-16 stand rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by Jarnigan in view of Dubrow and Kricka.

Claims 1, 2, and 25 are rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-3 of U.S. Patent 6,811,968. Claims 1 and 25 are rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 2, 5-7 and 11 of U.S. Patent 6,818,403. Claims 1, 2 and 25 are rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-3, 17 and 18 of U.S. Patent 6,982,171.

### **Summary of Arguments in Response to Rejection**

With regard to the first grounds of rejection, Kricka fails to disclose all the limitations of claim 1. Claim 1 recites the steps of, "providing a support member having *a smooth upper surface; removably sealing a top member to the smooth upper surface of the support member with substantially fluid tight, conformal contact to create a discrete assay chamber ...including...a channel region...wherein the channel region is exposed to the environment*". Kricka discloses a solid substrate (14) having a flow channel (20) formed in the top surface of the substrate (14), as shown in Figure 1. Thus, Kricka does not disclose a support member having a smooth upper surface as recited in claim 1, since the channel is formed in the top surface. Claim 1 recited that the first well, the second well, and the channel are formed by the top member in conjunction with the smooth surface of the support member. Furthermore, the channels in Kricka are not exposed to the environment, as the "cover to the substrate...closes the channel" (col 3, line 62). In the Advisory Action of August 9, 2007, the Examiner admits that the channels of Kricka are "formed within the interior of the device," but he argues that "the channels are still exposed to the environment because they are in fluid communication with the inlet and outlet ports." Although the material in the channel may be exposed to the environment, the channel region itself is not, as it is covered and is in the interior of the device. Additionally, the Examiner admits that Kricka's cover

is not configured to be removably sealed (Final Rejection, page 3). Kricka's cover (12) is clamped or otherwise bonded to the substrate (14) (col 13, lines 45-47), thus is not removable. Additionally, Kricka does not disclose any kind of conformal contact between the substrate and the cover. As described in the instant specification, conformal contact means "substantially form-fitting contact" (see page 11). The cover of Kricka is simply placed on top of the substrate and permanently bonded, and therefore does not "conform".

Dubrow fails to cure the deficiencies of Kricka. Dubrow shows a microfluidic device with a lower layer (110) and an upper layer (102). The lower layer does not have a smooth upper surface, as recited in claim 1, but rather has a plurality of grooves and wells (114) on the surface. Furthermore, the channels in Dubrow are explicitly enclosed below the cover layer so the channels are formed within the interior of the device (col 3, lines 28-32), and thus the channels are not exposed to the environment. Additionally, the Examiner references Fig. 1 to suggest the upper layer (102) and lower layer (110) are in form-fitting conformal contact. However, there is no disclosure of form-fitting conformal contact; rather Dubrow's device includes small high spots (214) to prevent the two layers from fully touching, to allow adhesive to flow in between (col 10, lines 22-29). Although the Examiner argues in the Advisory Action that the small high spots are not present in the embodiment of Figure 1, the disclosure as a whole teaches away from conformal contact, since adhesive bonding described as a preferred method. Similar to Kricka, the two layers are placed on top of each other and permanently bonded with adhesive bonding, UV or solvent welding, thermal bonding, or mechanical clamps. If mechanical clamps are used, as shown in Fig. 3B, a gasket (314) is provided between the upper and lower layers, and thus there is still no "form-fitting conformal contact" as defined in the present specification. The cover of Dubrow is simply placed on top of the substrate and permanently bonded, similarly to Kricka, and therefore does not "conform".

Kricka and Dubrow, alone or together, do not disclose all of the limitations of claim 1. For at least these reasons, Applicants submit that claim 1 (and all claims that depend therefrom) are not obvious over Kricka and Dubrow and Applicants respectfully request withdrawal of this rejection.

With regard to the second grounds of rejection, Jarnigan fails to disclose all the limitations of claim 1. Claim 1 recites the steps of, "providing a support member having a *smooth upper surface*; *removably* sealing a top member to the smooth upper surface of the support member with substantially fluid tight, *conformal contact* to create a discrete assay chamber ...including...a channel region...wherein *the channel region is exposed to the environment*". Jarnigan discloses a housing with a plurality of chambers and channels therebetween, as shown in figure 5A. However, the Examiner admits that Jarnigan "does not expressly indicate that a top member is removably sealed to a support member with substantially tight, conformal contact." In fact, Jarnigan does not disclose any top member, except in the embodiment of Figure 1, which cannot be combined with the embodiment of Figure 5. Even in the

embodiment of Figure 1, the cover plate is sealed to the top surface of the ridge (see col. 5, lines 28-30) and thus does not have form-fitting conformal contact with the base member and only contacts the top surface of the ridge of the base member. Additionally, in the embodiment of Figure 1, the channels are enclosed beneath the cover member and thus are not exposed to the environment. Jarnigan also fails to disclose a smooth top surface of the support member, since the channels and wells are formed in the top surface of the support member as shown in Figure 5A. Although the channels of Jarnigan are exposed to the environment in the embodiment of Figure 5, that is only because there is no top member. Furthermore, Jarnigan cannot disclose that the top member is removably sealed in form-fitting conformal contact, because there is no top member.

Dubrow fails to cure the deficiencies of Jarnigan. Even if the top member of Dubrow was added to the device of Jarnigan, for which there is no teaching or suggestion, the combination would still fail to disclose all the limitations of claim 1. As discussed above, Dubrow fails to disclose a smooth top surface of the support member, removably sealing a top member with conformal contact, and a channel exposed to the environment. For at least these reasons, Applicants submit that claim 1 (and all claims that depend therefrom) are not obvious over the combination of Jarnigan and Dubrow and respectfully request withdrawal of this rejection.

With regard to the third grounds of rejection, neither Kricka or Jarnigan, alone or in combination with Dubrow, teach all of the limitations of claim 1, as discussed above. Furthermore, Goodwin Jr. does not cure these deficiencies. Goodwin Jr. describes chemotaxis test sites with top and bottom regions separated by a membrane filter, and thus does not describe a support member with a removably sealable top member as claimed. For at least these reasons, Applicants submit that claims 3-5 are not rendered obvious by the combination of Kricka or Jarnigan, and Dubrow and Goodwin, Jr. and Applicants request withdrawal of this rejection.

With regard to the fourth grounds of rejection, Jarnigan and Dubrow do not teach all of the limitations of claim 1, as discussed above, and Kennedy and/or Shonnard do not cure these deficiencies. Kennedy and/or Shonnard do not describe a support member with a removably sealable top member as claimed. Shonnard describes chemotaxis experiments using a known Palleroni chamber and Kennedy uses small test tubes for his experiments. For at least these reasons, Applicants submit that claims 3-5, 12, 13 and 19-23 are not rendered obvious by the combination of Jarnigan, Dubrow, and Kennedy and/or Shonnard and Applicants request withdrawal of this rejection.

With regard to the fifth grounds of rejection, as discussed above, Kricka or Jarnigan and Dubrow, alone or in combination, do not disclose all of the limitations of claim 1, and Jeon cannot cure this deficiency. Jeon does not describe a support member with a removably sealable top member, where the channel region is exposed to the environment as claimed. The channel (240) in Jeon (Fig. 6) is covered

by the top member and thus is not exposed to the environment. Additionally, Jeon discloses that the top member and the support member can be sealed with a sealant or adhesive (col 11, lines 63-64), thus the top member is not removably sealed. For at least these reasons, Applicants submit that claims 3 and 6-8 are not rendered obvious by the combination of Kricka or Jarnigan, Dubrow, and Jeon, and Applicants request withdrawal of this rejection.

With regard to the sixth grounds of rejection, as discussed above, Kricka, Jarnigan and Dubrow, alone or in combination, do not disclose all of the limitations of claim 1. For at least these reasons, Applicants submit that claims 14-16, which depend from claim 1 either directly or indirectly, are not rendered obvious by the combination of Jarnigan and Kricka, and Applicants request withdrawal of this rejection.

With respect to the seventh grounds of rejection, claim 25 was previously cancelled, thus the rejection of this claim is moot. Applicants request that these rejections of claims 1 and 2 be held in abeyance until an indication of allowable subject matter has been made.

### CONCLUSION

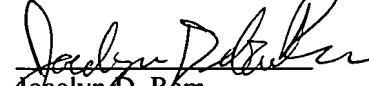
In view of the foregoing, the Examiner erred in finally rejecting claims 1-24. Accordingly, favorable action on this Pre-Appeal Brief Request for Review is respectfully requested.

Any fees for extension(s) of time or additional fees required in connection with the filing of this response, are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

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Respectfully submitted,  
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